

REMARKS

The Applicants acknowledge the Examiner's comprehensive Office Action with appreciation. The Office maintains the previously issued Restriction Requirement. Claims 9-16 remain pending in the application; however, method Claim 16 has been withdrawn as a result of the Restriction Requirement. The Office raises a prior art rejection under 35 USC § 103. The Office also raises a formalistic objection.

With regard to the previously issued Restriction Requirement, the Office acknowledges the Applicants' election with traverse to prosecute the compositions of **Group I**; however, the Office has refused the Applicants' request that, in accordance with PCT Rule 13.2, the Office include at least one method of treatment claim from **Group II** for simultaneous prosecution with the substance claims of **Group I**. The Office goes on to state that the instant claims lack a common special technical feature because the special technical feature of **Group I** is a "composition" and the special technical feature of **Group II** is a "method of using said composition." This statement is in contrast to the Office statement in the Restriction Requirement that **Groups I and II** lack unity of invention because the shared common technical feature (arbitrarily defined by the Office as the compound of formula I, which compound the Office stated was disclosed in US Patent No. 5,472,979) does not define a contribution over the prior art. Therefore, the Applicants submit contemporaneously with the instant Response a Petition from the Requirement for Restriction.

In the absence of a favorable decision on the above-mentioned Petition from the Requirement for Restriction, the Applicants request that, in accordance with MPEP § 821.04, the Office rejoin non-elected method Claim 16 upon the identification of allowable subject matter.

Claims 9-15 are rejected for obviousness under 35 USC § 103(a) based on the disclosure of Lavielle, et al. (US Patent No. 5,472,979) in view of Helgason, et al. It is the position of the Office that Lavielle, et al. disclose that the instant compound of formula (I) is capable of inhibiting platelet aggregation. The Office acknowledges that the Lavielle, et al. reference does not disclose combining the compound of

formula (I) with aspirin and that the cited reference also does not disclose a compound of formula (I) having the (R) configuration. It is the further position of the Office that Helgason, et al. disclose a combination therapy consisting of aspirin and clopidogrel as a treatment regimen for the inhibition of platelet aggregation.

The Office concludes that, based on the disclosure of Helgason, et al. one skilled in the art would have been motivated to combine the platelet aggregation inhibitor of formula (I) with aspirin with a reasonable expectation of success that such a combination would be effective for the inhibition of platelet aggregation. With respect to the instantly claimed combinations comprising the (R) isomer of the compound of formula (I), it is the position of the Office that one skilled in the art would recognize that the individual isomers of the compound of formula (I) would have different activity. The Office goes on to state that one skilled in the art would have known how to resolve a racemic mixture of the compound of formula (I) and would have been motivated to do so with the expectation that the enantiomers would have substantially different pharmacological activity.

The Applicants respectfully submit that the Helgason, et al. reference discloses (based on *ex vivo* platelet aggregation studies) that the combination of clopidogrel and aspirin, while effective in inhibiting platelet aggregation, only exhibits synergistic interaction between the two drugs when epinephrine is the aggregation agonist. The reference further discloses that incompatibility was observed when adenosine diphosphate was used as the agonist and that a mixed response of additivity and incompatibility was observed when either arachidonic acid or collagen were used as the agonists. The disclosed results are, at best, inconclusive with respect to the effects of the disclosed combinations. Therefore, the ambiguous disclosure of Helgason, et al. (which suggests both positive and negative results associated with the disclosed combinations) actually teaches away from the instantly claimed combinations. One skilled in the art would not have been motivated to combine the disclosure of Lavielle, et al. with the ambiguous disclosure of Helgason, et al. to arrive at the instantly claimed combinations.

Moreover, the instant specification discloses (at pages 2 and 4-5) that the instantly claimed combination exhibits synergistic effects in terms of anti-thrombotic activity compared to monotherapy and that this synergistic effect has been demonstrated in an arterial thrombosis model, with specific disclosure at page 5 that, in the presence of a dose of aspirin which does not produce an anti-thrombotic effect, the anti-thrombotic effect of the compound of formula (I) is potentiated and increased by about 30 times. The Applicants respectfully submit that there is no teaching in either of the cited references (alone or in combination) to suggest the synergistic effects associated with the instantly claimed combinations. Reconsideration and withdrawal of the obviousness rejection is respectfully requested.

Finally, the Office objects to Claim 16 as having an improper status identifier. With the instant Amendment, Claim 16 is indicated as "withdrawn." Withdrawal of the objection and rejoinder of Claim 16 is respectfully requested.

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Accordingly, entry of the present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, rejoinder of the non-elected method claim, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned agent has made an earnest effort to place this application into condition for immediate allowance. If she can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call her at her below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

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Enclosure: Listing of Claims and Postal Card Receipt

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.